

CLAIMS

1. A device for reading and analyzing chips,
comprising:
 - 5 • a table for receiving a chip intended to characterize at least one sample,
 - means of exciting the molecules or the cells of the chip, after reaction with other molecules,
 - 10 • means of reading and analyzing the molecules subjected to excitation,characterized in that the device also comprises:
 - 15 • a unit for controlling the temperature of said table, said control unit being connected to a module (111) consisting of a plurality of Peltier-type heating/cooling elements arranged opposite various spots on the surface of the table,
 - and at least one table temperature sensor (112) also connected to said control unit.
- 20 2. The device as claimed in the preceding claim, characterized in that the excitation means comprise a broad-spectrum lamp and at least one laser.
- 25 3. The device as claimed in either of the preceding claims, characterized in that the laser is a laser whose radiation is centered on a wavelength of the order of 635 nm.
- 30 4. The device as claimed in one of the preceding claims, characterized in that the reader comprises several lasers.
- 35 5. The device as claimed in the preceding claim, characterized in that the lasers are centered on the same wavelength.

6. The device as claimed in one of the preceding claims, characterized in that the excitation means comprise at least one laser associated with a module for scanning of its beam so as to excite the molecules to be analyzed.
7. The device as claimed in the preceding claim, characterized in that the reader comprises two lasers and the modules for scanning of the two lasers control two respective scans of the molecules in two orthogonal directions.
8. The device as claimed in one of claims 1 to 5, characterized in that the excitation means comprise at least one laser assembly comprising a laser whose radiation is guided by an optical fiber.
9. The device as claimed in the preceding claim, characterized in that the excitation means comprise two identical laser assemblies.
10. The device as claimed in one of claims 1 to 5, characterized in that the excitation means comprise a fixed laser (132") which directs its beam toward two successive mirror assemblies mounted in series, and the movement of which is controlled along two different directions.
11. The device as claimed in the preceding claim, characterized in that the movement of the two mirror assemblies is controlled so as to produce a beam which can follow any desired sequence on the chip.
12. The device as claimed in one of claims 1 to 5, characterized in that the excitation means comprise a lamp and a laser whose radiations

follow the same optical path due to a swinging mirror (130) that can pivot around an axis (1300) between two positions so as to direct one of these two radiations toward the chip.

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13. The device as claimed in one of the preceding claims, characterized in that an optical system is interposed between the lamp and the molecules to be excited, whereas the laser excitation takes place by direct illumination of the molecules.

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14. The device as claimed in the preceding claim, characterized in that said optical system comprises narrow bandwidth excitation light filters and narrow bandwidth emission light filters, and a beam separator.

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15. The device as claimed in one of the preceding claims, characterized in that the reader also comprises an excitation control unit connected to each of the excitation means in order to control the functioning thereof.

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16. The device as claimed in the preceding claim, characterized in that said excitation control unit is capable of selectively controlling the simultaneous or successive illumination of the molecules with the lamp and at least one laser, or the separate excitation of the molecules with the lamp and at least one laser.

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17. A device for reading and analyzing chips, comprising:

- a table for receiving a chip intended to characterize at least one sample,
- means of exciting the cells or molecules of the chip, after reaction with other molecules or cells,
- means of reading the molecules or cells

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subjected to excitation,
characterized in that the reader also comprises a
temperature control unit.

- 5 18. The device as claimed in the preceding claim,
characterized in that the table comprises a
temperature sensor connected to said temperature
control unit.
- 10 19. The device as claimed in either of the two
preceding claims, characterized in that the reader
comprises a heating/cooling module associated with
the table and intended to control its temperature,
said heating/cooling module being connected to the
15 temperature control unit.
- 20 20. The device as claimed in one of the three
preceding claims, characterized in that the reader
also comprises processing means comprising a
20 microprocessor and connected to the temperature
control unit and also to the reading means.
- 25 21. The device as claimed in the preceding claim,
characterized in that the reader comprises means
of storing reference curves of the response of the
matches and mismatches of the molecules to the
excitation means as a function of the temperature.
- 30 22. The device as claimed in the preceding claim,
characterized in that the storage means are
connected to means for determining a melting
temperature for the matches and mismatches of the
molecules, from said reference curves.
- 35 23. The device as claimed in one of the six preceding
claims, characterized in that the temperature
control unit is capable of controlling the
functioning of the reader according to a "static"
mode in which pre-established reference curves of

the response of the matches and mismatches of the molecules as a function of the temperature are used to establish a set temperature that can be transmitted, by said temperature control unit, so
5 as to control the temperature of said table.

24. The device as claimed in one of the seven preceding claims, characterized in that the temperature control unit is capable of controlling
10 the functioning of the reader according to a "dynamic" mode in which the temperature control unit controls a given change in temperature on the table, and, during this change in temperature:

- 15 • the reading means collect, in real time, the response of the molecules associated with the various spots on the chip to the excitation by the excitation means, and transmit said response to processing means (18),
- 20 • storage means store, for each spot on the chip, the change in response of the molecule as a function of the temperature.

25. The device as claimed in the preceding claim, characterized in that the reader comprises
25 processing means capable of establishing, for each molecule, at the end of the storage of said change in response, a diagnosis of state of the molecule.

26. The device as claimed in the preceding claim,
30 characterized in that said diagnosis of state is a match/mismatch diagnosis.

27. A method of hybridization of the oligonucleotides of a chip, which can be carried out by means of a
35 reader as claimed in one of the preceding claims, the method comprising the steps consisting in:

- bringing the nucleic acid probes corresponding to a target nucleic acid into contact with a biological sample containing single-stranded

DNA fragments, so as to carry out a selective hybridization of certain probes with said single-stranded DNA fragments of the sample, by forming duplexes,

- 5 • reading the duplexes thus formed, characterized in that the method comprises a step consisting of automatic determination of:
 - the melting temperature for each target nucleic acid in a "match" configuration, and
 - 10 • the melting temperature for each target nucleic acid in a "mismatch" configuration.

28. The method as claimed in the preceding claim, characterized in that said determination is
15 carried out in the "static" mode using reference curves illustrating the change, as a function of the temperature, in the signal received by means of reading duplexes corresponding, respectively, to matches and to mismatches.

20 29. The method as claimed in the preceding claim, characterized in that the method comprises controlling the temperature so as to carry out the hybridization at a temperature corresponding to a
25 maximum distinction between match and mismatch.

30. The method as claimed in the preceding claim, characterized in that the method comprises producing said reference curves during a step that
30 precedes the reading step.

31. The method as claimed in the preceding claim, characterized in that the method comprises storing said reference curves.

35 32. The method as claimed in one of the five preceding claims, characterized in that said determination can be carried out in the "dynamic" mode by controlling a given change in temperature of the

samples, and, during this change in temperature, the following are carried out:

- 5 • real-time collection of the response of the duplexes associated with the various spots on the chip to the excitation by the excitation means,
- for each duplex, storage of the change in the response as a function of the temperature.

10 33. The method as claimed in the preceding claim, characterized in that the method comprises, for each duplex, establishing, at the end of the storage of said change in response, a diagnosis of match/mismatch of the duplex.